

In the Claims

Please amend the claims as follows.

1. (Currently Amended) A method comprising:
identifying an agent that contacted with a mammalian cell which agent enhances adeno-associated virus transduction of a the mammalian cell after viral binding to the cell membrane and before second strand synthesis which yields an expressible form of the viral genome, wherein the agent enhances adeno-associated virus transport to the nucleus.
2. (Previously Presented) The method of claim 1 or 87 wherein the cell is a mammalian lung cell.
3. (Previously Presented) The method of claim 1 or 87 wherein the cell is a mammalian liver cell.
4. (Previously Presented) The method of claim 1 or 87 wherein the cell is a human cell, canine cell, murine cell, rat cell or rabbit cell.
5. (Previously Presented) The method of claim 1 or 87 wherein the transduction is enhanced before uncoating of viral particles.
6. (Previously Presented) The method of claim 1 or 87 wherein the agent enhances endosomal processing.
7. (Previously Presented) The method of claim 1 or 87 wherein the agent is an endosomal protease inhibitor.
8. (Original) The method of claim 7 wherein the agent is a cysteine protease inhibitor.

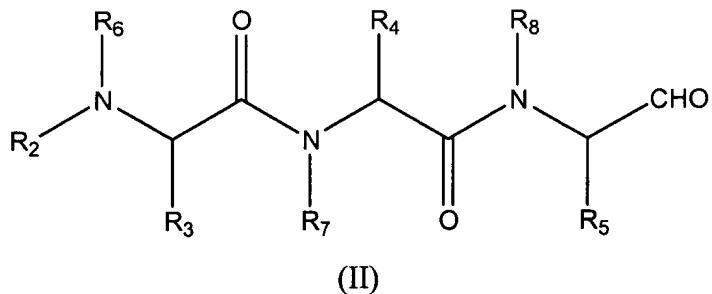
9. (Previously Presented) The method of claim 1 or 87 wherein the agent is a peptide or analog thereof.
10. (Previously Presented) The method of claim 1 or 87 wherein the virus is recombinant adeno-associated virus.
11. (Original) The method of claim 10 wherein the recombinant virus encodes a therapeutic peptide or polypeptide.
12. (Previously Presented) The method of claim 10 wherein the recombinant virus comprises a marker gene that is detectable or selectable.
- 13-28. (Cancelled)
29. (Previously Presented) The method of claim 1 or 87 wherein the agent is a compound of formula (I): R₁-A-(B)_n-C wherein R₁ is an N-terminal amino acid blocking group; each A and B is independently an amino acid; C is an amino acid wherein the terminal carboxy group has been replaced by a formyl (CHO) group; and n is 0, 1, 2, or 3; or a pharmaceutically acceptable salt thereof.
30. (Original) The method of claim 29 wherein R₁ is (C₁-C₁₀)alkanoyl.
31. (Original) The method of claim 29 wherein R₁ is acetyl or benzyloxycarbonyl.
32. (Original) The method of claim 29 wherein each A and B is independently alanine, arginine, glycine, isoleucine, leucine, valine, nor-leucine or nor-valine.
33. (Original) The method of claim 29 wherein each A and B is isoleucine.

34. (Original) The method of claim 29 wherein C is alanine, arginine, glycine, isoleucine, leucine, valine, nor-leucine or nor-valine, wherein the terminal carboxy group has been replaced by a formyl (CHO) group.

35. (Original) The method of claim 29 wherein C is nor-leucine or nor-valine, wherein the terminal carboxy group has been replaced by a formyl (CHO) group.

36. (Original) The method of claim 29 wherein R₁ is (C₁-C₁₀)alkanoyl or benzyloxycarbonyl; A and B are each isoleucine; C is nor-leucine or nor-valine, wherein the terminal carboxy group has been replaced by a formyl (CHO) group; and N is 1.

37. (Withdrawn) The method of claim 1 or 87 wherein the agent is a compound of formula (II):



wherein

R₂ is an N-terminal amino acid blocking group;

R₃, R₄, and R₅ are each independently hydrogen, (C₁-C₁₀)alkyl, aryl or aryl(C₁-C₁₀)alkyl; and

R₆, R₇, and R₈ are each independently hydrogen, (C₁-C₁₀)alkyl, aryl or aryl(C₁-C₁₀)alkyl; or a pharmaceutically acceptable salt thereof.

38. (Withdrawn) The method of claim 37 wherein R₂ is (C₁-C₁₀)alkanoyl.

39. (Withdrawn) The method of claim 37 wherein R₂ is acetyl or benzyloxycarbonyl.

40. (Withdrawn) The method of claim 37 wherein R₃ is hydrogen or (C₁-C₁₀)alkyl.

41. (Withdrawn) The method of claim 37 wherein R₃ is 2-methylpropyl.

42. (Withdrawn) The method of claim 37 wherein R₄ is hydrogen or (C₁-C₁₀)alkyl.

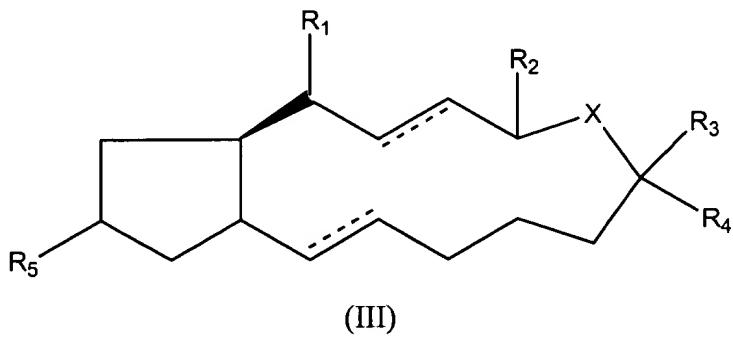
43. (Withdrawn) The method of claim 37 wherein R₄ is 2-methylpropyl.

44. (Withdrawn) The method of claim 37 wherein R₅ is hydrogen or (C₁-C₁₀)alkyl.

45. (Withdrawn) The method of claim 37 wherein R₅ is butyl or propyl.

46. (Withdrawn) The method of claim 37 wherein R₂ is acetyl or benzyloxycarbonyl; R₃ and R₄ are each 2-methylpropyl; R₅ is butyl or propyl; and R₆, R₇, and R₈ are each independently hydrogen.

47. (Withdrawn) The method of claim 1 or 87 wherein the agent is a compound of formula (III):



wherein

R₁ is H, halogen, (C₁-C₁₀)alkyl, (C₁-C₁₀)alkenyl, (C₁-C₁₀)alkynyl, (C₁-C₁₀)alkoxy, (C₁-C₁₀)alkanoyl, (=O), (=S), OH, SR, CN, NO₂, trifluoromethyl or (C₁-C₁₀)alkoxy, wherein any alkyl, alkenyl, alkynyl, alkoxy or alkanoyl may optionally be substituted with one or more halogen, OH, SH, CN, NO₂, trifluoromethyl, NRR or SR, wherein each R is independently H or (C₁-C₁₀)alkyl;

R₂ is (=O) or (=S);

R₃ is H, (C₁-C₁₀)alkyl, (C₁-C₁₀)alkenyl, (C₁-C₁₀)alkynyl, (C₁-C₁₀)alkoxy or (C₃-C₈)cycloalkyl, wherein any alkyl, alkenyl, alkynyl, alkoxy or cycloalkyl may optionally be substituted with one or more halogen, OH, CN, NO₂, trifluoromethyl, SR, or NRR, wherein each R is independently H or (C₁-C₁₀)alkyl;

R₄ is H, (C₁-C₁₀)alkyl, (C₁-C₁₀)alkenyl, (C₁-C₁₀)alkynyl, (C₁-C₁₀)alkoxy or (C₃-C₈)cycloalkyl, wherein any alkyl, alkenyl, alkynyl, alkoxy or cycloalkyl may optionally be substituted with one or more halogen, OH, CN, NO₂, trifluoromethyl, SR, or NRR, wherein each R is independently H or (C₁-C₁₀)alkyl;

R₅ is H, halogen, (C₁-C₁₀)alkyl, (C₁-C₁₀)alkenyl, (C₁-C₁₀)alkynyl, (C₁-C₁₀)alkoxy, (C₁-C₁₀)alkanoyl, (=O), (=S), OH, SR, CN, NO₂ or trifluoromethyl, wherein any alkyl, alkenyl, alkynyl, alkoxy or alkanoyl may optionally be substituted with one or more halogen, OH, SH, CN, NO₂, trifluoromethyl, NRR or SR, wherein each R is independently H or (C₁-C₁₀)alkyl; and

X is O, S or NR wherein R is H or (C₁-C₁₀)alkyl, or a pharmaceutically acceptable salt thereof.

48. (Withdrawn) The method of claim 47 wherein R₁ is halogen, CN, NO₂, trifluoromethyl or OH.

49. (Withdrawn) The method of claim 47 wherein R₁ is OH.

50. (Withdrawn) The method of claim 47 wherein R₂ is (=O).

51. (Withdrawn) The method of claim 47 wherein R₃ is H or (C₁-C₁₀)alkyl.

52. (Withdrawn) The method of claim 47 wherein R₃ is methyl.

53. (Withdrawn) The method of claim 47 wherein R₄ is H or (C₁-C₁₀)alkyl.

54. (Withdrawn) The method of claim 47 wherein R₄ is H.

55. (Withdrawn) The method of claim 47 wherein R₅ is halogen, CN, NO₂, trifluoromethyl or OH.

56. (Withdrawn) The method of claim 47 wherein R₅ is OH.

57. (Withdrawn) The method of claim 47 wherein X is O or S.

58. (Withdrawn) The method of claim 47 wherein X is O.

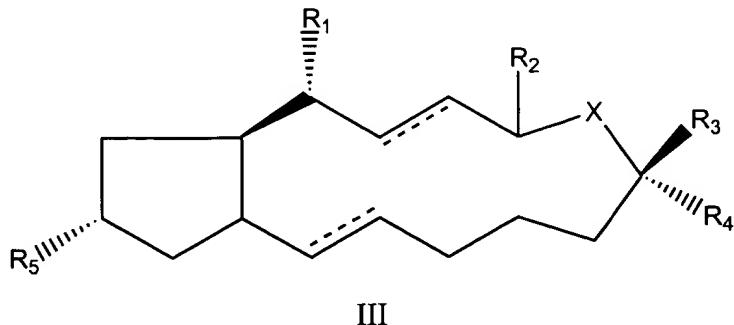
59. (Withdrawn) The method of claim 47 wherein both ----- are a single bond.

60. (Withdrawn) The method of claim 47 wherein one ----- is a double bond.

61. (Withdrawn) The method of claim 47 wherein both ----- are a double bond.

62. (Withdrawn) The method of claim 45 wherein R₁ is OH, R₂ is (=O), R₃ is methyl, R₄ is H, R₅ is OH, X is O, and both ----- are a double bond.

63. (Withdrawn) The method of claim 47 wherein the compound is a compound of formula (III):



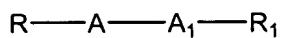
64. (Withdrawn) The method of claim 63 wherein R₁ is halogen, CN, NO₂, trifluoromethyl or OH.

65. (Withdrawn) The method of claim 63 wherein R₁ is OH.
66. (Withdrawn) The method of claim 63 wherein R₂ is (=O).
67. (Withdrawn) The method of claim 63 wherein R₃ is H or (C₁-C₁₀)alkyl.
68. (Withdrawn) The method of claim 63 wherein R₃ is methyl.
69. (Withdrawn) The method of claim 63 wherein R₄ is H or (C₁-C₁₀)alkyl.
70. (Withdrawn) The method of claim 63 wherein R₄ is H.
71. (Withdrawn) The method of claim 63 wherein R₅ is halogen, CN, NO₂, trifluoromethyl or OH.
72. (Withdrawn) The method of claim 63 wherein R₅ is OH.
73. (Withdrawn) The method of claim 63 wherein X is O or S.
74. (Withdrawn) The method of claim 63 wherein X is O.
75. (Withdrawn) The method of claim 63 wherein both ----- are a single bond.
76. (Withdrawn) The method of claim 63 wherein one ----- is a double bond.
77. (Withdrawn) The method of claim 63 wherein both ----- are a double bond.
78. (Withdrawn) The method of claim 63 wherein R₁ is OH, R₂ is (=O), R₃ is methyl, R₄ is H, R₅ is OH, X is O, and both ----- are a double bond.

79. (Withdrawn) The method of claim 1 or 87 wherein the agent inhibits the activation of ubiquitin, the transfer of ubiquitin to the ubiquitin carrier protein, ubiquitin ligase, or a combination thereof.

80. (Withdrawn) The method of claim 1 or 87 wherein the agent inhibits ubiquitin ligase.

81. (Withdrawn) The method of claim 1 or 87 wherein the agent is a compound of formula (IV):



wherein R is hydrogen, an amino acid, or a peptide, wherein the N-terminus amino acid can optionally be protected at the amino group with acetyl, acyl, trifluoroacetyl, or benzyloxycarbonyl; A is an amino acid or a direct bond; A₁ is an amino acid; and R₁ is hydroxy or an amino acid, wherein the C-terminus amino acid can optionally be protected at the carboxy group with (C₁-C₆)alkyl, phenyl, benzyl ester or amide (e.g., C(=O)NR₂, wherein each R is independently hydrogen or (C₁-C₆)alkyl); or a pharmaceutically acceptable salt thereof.

82. (Withdrawn) The method of claim 81 wherein the agent is H-Leu-Ala-OH, H-His-Ala-OH, or a combination thereof.

83. (Previously Presented) The method of claim 1 or 87 further comprising administering a second agent that enhances the activity of the agent.

84. (Original) The method of claim 83 wherein the second agent is EGTA.

85. (Canceled)

86. (Previously Presented) The method of claim 1 or 87 wherein the agent alters endosomal processing.

87. (Currently Amended) A method to identify an agent that enhances adeno-associated virus (AAV) transduction of a mammalian cell, comprising:
 - a) contacting the mammalian cell with one or more agents and adeno-associated virus; and
 - b) identifying at least one agent that enhances transduction after viral binding to the cell membrane and before second strand synthesis which yields an expressible form of the viral genome, wherein the agent enhances adeno-associated virus transport to the nucleus of the mammalian cell.
88. (New) A method comprising: identifying an agent contacted with a mammalian cell which enhances adeno-associated virus transport to the nucleus.
89. (New) A method to identify an agent that enhances adeno-associated virus transduction of a mammalian cell, comprising:
 - a) contacting the mammalian cell with one or more agents and adeno-associated virus; and
 - b) identifying at least one agent that enhances adeno-associated virus transport to the nucleus of the mammalian cell.